

Macrolide-resistant *Streptococcus pneumoniae* (SPN) in Argentina (ARG): prevalence of *ermB* and *mefA* genes

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From 1993 ARG has been participating in a national epidemiological surveillance conducted by PAHO, in order to determine the prevalence of capsular types and antimicrobial resistance patterns of SPN causing invasive infections in children ≤ 6 y-o.

From February 1993 to December 2001, a total of 1499 SPN clinical isolates were isolated from 44 hospitals and 17 cities in Argentina (FIG.1). In 1995, the first SPN showing resistance to erythromycin (ERY) was isolated. During the period of study, a total of 52 (3.5%) SPN were erythromycin-resistant (ERY-R), and resistance increased from 0% in 1993-4 to 1.4% in 1995-7 and 6% in 1998-2001.

This is the first National study describing the mechanisms of macrolides resistance in SPN from Argentina.

OBJECTIVES

To characterize the mechanism of macrolides-resistance in *S. pneumoniae* clinical isolates from Argentina.

MATERIALS AND METHODS

A total of 50 ERY R SPN strains, were available for the molecular characterization of the resistance mechanism. These were recovered from 14 hospitals and 8 cities (FIG.1). Thirty-one isolates (62%) were isolated from patients with pneumonia, 12 (24%) with meningitis and 7 (14%) with other infectious diseases. Serotypes were determined by Quellung and MICs by the agar dilution procedure (interpreted according to CLSI). Phenotypes of macrolides resistance was determined using ERY (15 μ g) and clindamycin (2 μ g) disks as previously described. PCR to detect *ermB* and *mefA* genes was performed under standard conditions. Clonal relationship was established by *Sma*I-PFGE.

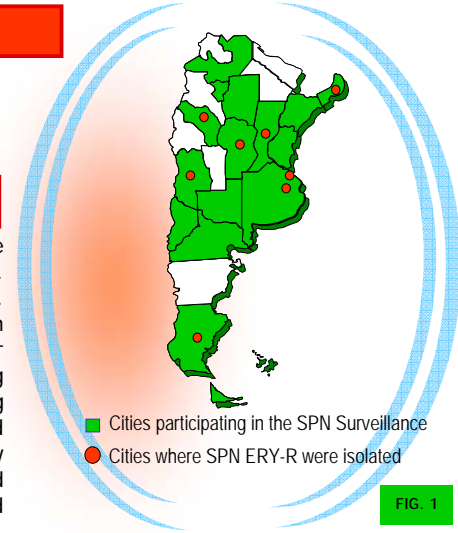


FIG. 1

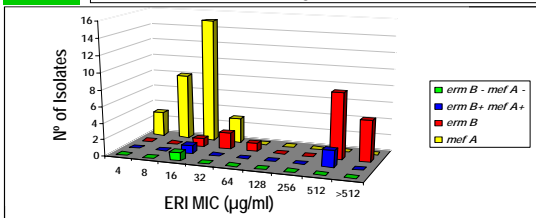
RESULTS

TABLE 1 GENOTYPE/PHENOTYPE of ERY-R SPN

GENOTYPE	N° isolates	PHENOTYPE		
		M	cMLS _B	iMLS _B
<i>mefA</i>	29 (58%)	29 (100%)	0	0
<i>ermB</i>	17 (34%)	0	17 (81%)	0
<i>mefA</i> + <i>ermB</i> +	3 (6%)	0	3 (14%)	0
<i>mefA</i> - <i>ermB</i> -	1 (2%)	0	1 (5%)	0
Total	50 (100%)	29 (58%)	21 (42%)	0

M phenotype: cMLS_B: constitutively; iMLS_B: inducibly

FIG. 2 ERY MIC by GENOTYPE



• ERY MIC range (in μ g/ml) in SPN *mefA*: 4-32, *ermB*: 16->512, *ermB*+*mefA*+: 16-512, and negative for both genes: 16 (FIG. 2)

TABLE 2 CLONAL TYPES / SEROTYPES / GENOTYPES

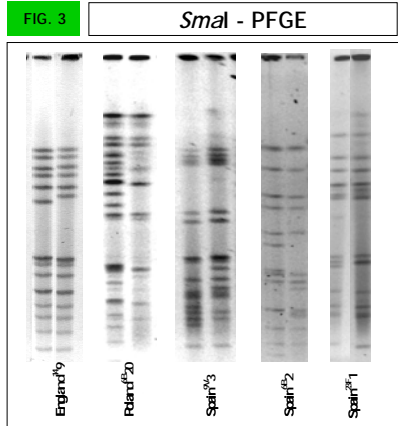
<i>Sma</i> I PFGE	International clone	N° of isolates (%)	SEROTYPE	N° of isolates (%)	GENOTYPE	N° of isolates
A	England ¹⁴ -9	21 (42)	14	17 (81)	<i>mefA</i>	17
			19A	1 (5)	<i>mefA</i>	1
			23A	1 (5)	<i>mefA</i>	1
			6B	2 (9)	<i>ermB</i> + <i>mefA</i> +	2
B	Poland ^{6B} -20	10 (20)	6B	10 (100)	<i>ermB</i> <i>mefA</i>	9 1
			C	Spain ^{9V} -3	8 (16)	14
9V	4 (50)	<i>mefA</i> <i>mefA</i> - <i>ermB</i> -	3 1			
D	Spain ^{6B} -2	3 (6)	6B	2	<i>ermB</i> <i>ermB</i>	2 1
			19F	1	<i>mefA</i>	1
E	Spain ^{23F} -1	2 (4)	23F	2	<i>ermB</i> + <i>mefA</i> + <i>ermB</i>	1 1
			F	3 (6)	6B	3
G		1 (2)	14	1	<i>mefA</i>	1
H		1 (2)	19F	1	<i>mefA</i>	1
I		1 (2)	11A	1	<i>ermB</i>	1

• A total of 9 clonal types were identified by *Sma*I-PFGE (types A to I) (TABLE 2).

• Most of the ERY-R SPN isolates (88%) were related to 5 international clones: England¹⁴-9 (42%), Poland^{6B}-20 (20%), Spain^{9V}-3 (16%), Spain^{6B}-2 (6%) and Spain^{23F}-1 (4%) (FIG. 3).

• Serotypes in ERY-R SPN were 14 (44%), 6B (34%), 9V (8%), 19F (4%), 23F (4%), 23A (2%), 19A (2%) and 11A (2%).

• The *mefA* gene was predominant in SPN serotype 14 (100%) and 9V (75%), whilst *ermB* was common in serotype 6B (82%).



CONCLUDING REMARKS

1. *mefA* gene (58%) was more frequently detected than *ermB* gene (34%) in ERY-R SPN from Argentina (TABLE 1)
2. Three isolates (6%) carried both *ermB* and *mefA* genes
3. 88% of the ERY-R SPN were related to 5 International clones: England¹⁴-9 (44%), Poland^{6B}-20 (18%), Spain^{9V}-3 (16%), Spain^{6B}-2 (6%) and Spain^{23F}-1 (6%)
4. The prevalence of ERY-R SPN in Argentina is still low, but the continuous national surveillance is important to know the efficacy of macrolides in our country.